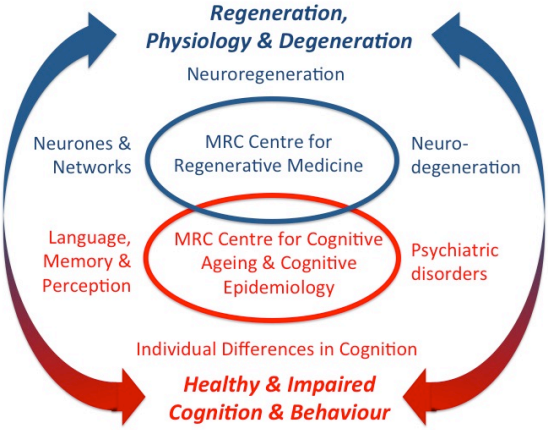
Institution: The University of Edinburgh

Unit of Assessment: UoA 4 Psychology, Psychiatry and Neuroscience

A. Overview

Research Organisation and Structure

Edinburgh Neuroscience (www.edinburghneuroscience.ed.ac.uk) is a vibrant, integrated, and interdisciplinary research structure launched at the University of Edinburgh (UoE) in 2006 to facilitate interaction between researchers across groups, centres, schools and colleges, working at all levels of neuroscience from molecules through synapses and networks to cognition and behaviour. 129 research staff are returned here. Our major strategic goal has been to bring together **Psychology, Psychiatry** and **Neuroscience** to target our basic and translational research on two of the key challenges for 21st century Neuroscience: **how does the human brain develop and function across the lifespan,** and **how can it be protected and repaired?**



In addressing these grand challenges, since RAE2008 we have organised our work in Edinburgh Neuroscience under two overarching cross-disciplinary themes, as shown in the Figure (left), (**Regeneration, Physiology and Degeneration; Healthy and Impaired Cognition and Behaviour)**. These themes are nucleated around two prestigious MRC Centres, both awarded in 2008 and both successfully renewed in 2013. The research synergy between the two main themes and the MRC Centres is delivered through six sub-themes, (Neuroregeneration; Neurones & Networks; Neurodegeneration; Individual Differences in Cognition; Language, Memory & Perception; Psychiatric Disorders), which drive discovery science and both clinical and non-clinical translational research through the lifespan. Each is led by internationally leading senior researchers from Psychology, Psychiatry or Neuroscience backgrounds. The key strength of our approach lies in bringing together colleagues working on the development, structure and function of the normal brain and its healthy ageing with clinician scientists and neuroscientists focussed on neurodevelopmental and neurodegenerative disease as well as repair (regeneration). Our basic neuroscience feeds forward into research on language development and use, links between lifestyle and health, public dissemination of science and also into the pathogenesis, cognitive/behavioural sequelae, assessment and potential therapy of conditions such as motor neurone disease (MND), multiple sclerosis (MS), psychosis, stroke and the dementias. At the same time, the study of these and other clinical conditions and of cognition and behaviour in everyday life feeds back into theoretical and empirical research on healthy neurophysiology, neuroregeneration, cognition and behaviour. The result is a powerful platform for interdisciplinary research advancing understanding of cognition, language, memory, perception and neurophysiology across the lifespan and devising novel strategies for the investigation and treatment of neurological disease.

Theme 1) Regeneration, Physiology & Degeneration

Within this theme the **MRC Centre for Regenerative Medicine** (Director, ffrench-Constant, also Director Edinburgh Neuroscience) acts as a research hub facilitating and interacting with major groups within each of the three sub-themes addressing the basic and clinical science of:

- Neuroregeneration (led by Brophy), incorporating the philanthropically funded Anne Rowling Regenerative Neurology Clinic and the charity funded MS Society Edinburgh Centre for Translational Research (co-led by Chandran and ffrench-Constant);
- Neurones & Networks, incorporating integrative physiology (led by Shipston);
- Neurodegeneration incorporating clinical brain sciences (led by Chandran), human cognitive neuroscience (led by Della Sala) and the philanthropically funded Euan MacDonald Centre for Motor Neurone Disease Research (led by Chandran).

Theme 2) Healthy and Impaired Cognition and Behaviour Across the Lifespan

Within this theme the **MRC Centre for Cognitive Ageing and Cognitive Epidemiology** (Director, Deary), acts as a research hub for major groups that focus on each of the three sub-themes addressing the basic and translational science of:

- Individual Differences in Cognition (led by Deary) incorporating the charity funded Alzheimer Scotland Dementia Research Centre (led by Starr);
- Language, Memory & Perception incorporating human cognition and behaviour (led by Logie) and cognitive and neural systems in animal models (led by Morris);
- Psychiatric Disorders, incorporating psychiatry (led by Lawrie), clinical psychology (led by Schwannauer), the philanthropically funded Patrick Wild Centre for Research into Autism, Fragile X Syndrome & Intellectual Disabilities (led by Kind & Stanfield) and Sackler Centre for Developmental Psychobiology (led by A McIntosh).

B. Research strategy

B1: Strategic Developments since 2008

Edinburgh Neuroscience was established in 2006 as the culmination of a 20-year process of integration across neurosciences in Edinburgh. Research has been organised by research themes, the development of which has been deliberately cross-cutting to address major scientific challenges, bringing research staff together in new interfaces regardless of other affiliations, with theme leadership provided by senior researchers. Since 2008, Psychology, Psychiatry and Neuroscience research has been underpinned by:-

- **£71.8M in infrastructure investment**, including the £56M Scottish Centre for Regenerative Medicine building, a £12.8M Anne Rowling Regenerative Neurology Clinic development and £3M to create a cognitive neuroscience laboratory suite within the new Dugald Stewart building, plus major refurbishment of the existing Psychology building with new and substantially upgraded laboratories for studying infant language development, psycholinguistics, human memory, and attention and perception;
- **Strategic recruitment of 19 new chairs and 29 Edinburgh Scientific Academic Track researchers** (see below);
- **Two funded and renewed MRC Centres** (Centre for Cognitive Ageing & Cognitive Epidemiology; Centre for Regenerative Medicine) (£11.5M awarded since 2008 with a further £26.7 invested by the University);
- **£90.4M in total external grant spend**, including £11.5M in 9 programme grants, £17.5M in charity and philanthropic funding (£2.2M MS Society Centre; £0.75M Alzheimer Scotland Dementia Research Centre; £12.8M Anne Rowling Regenerative Neurology Clinic (including new build above); £1.7M Shirley Foundation and other donations to the Patrick Wild Centre);
- **Major new drive in research training** including:
  - PsySTAR, a psychiatry postgraduate training scheme unique to the UK, initiated with £2.15M from Medical Research Council/Medical Research Foundation, led by Lawrie;
  - Edinburgh Clinical Academic Training (ECAT) scheme providing doctoral and post-doctoral training for clinician scientists; £6.2M (2008–12) plus £6.2M renewal in 2013 from the Wellcome Trust (WT); 20% ECAT trainees undertake neuroscience research projects;
  - Establishment of 29 new internationally recruited tenure track positions, and the development of the Edinburgh Scientific Academic Track (ESAT, which includes UoE Chancellor's Fellowship positions), a sector-leading career structure for non-clinical academics (~£2M UoE investment in this UoA; ongoing programme of recruitment in 2014);
  - ESRC Doctoral Training Centre pathways for Psychology and for Language Sciences within the Scottish Graduate School of Social Science.

Within UoE's highly collaborative environment are numerous other important links, as shown in this document and in REF2 and REF3, with other large research groups in medicine (UoA1), neuro-infection (UoA6), informatics (UoA11) and linguistics (UoA28), all bringing enormous added value to the UoA's research.

B2 Research Themes

Below, the major research aims and achievements of each theme in the REF period are described:

B2.1. Regeneration, Physiology and Degeneration

With 67 Cat A and 2 Cat C staff, research in this theme spans neurodevelopment and regeneration to mechanisms of normal function in the nervous system at the molecular, synaptic and network/systems level, and conditions resulting from degeneration such as MND, stroke and dementia. It has the MRC Centre for Regenerative Medicine as a major research hub and covers research on the three sub-themes of Neuroregeneration, Neurones & Networks and Neurodegeneration.

The MRC Centre for Regenerative Medicine [Director, ffrench-Constant; 2008: £2.4M from MRC, with an additional £15.5M from the University; in 2013: £2.2M from the MRC, £6.2M from the University] aligns our regenerative and developmental neuroscientists in neuroregeneration and neurones and networks with stem cell and inflammation biologists. Crucially, this includes those working in other tissues, notably liver and blood, who study the fundamental processes at the core of tissue regeneration (returned in UoA1), co-located within a new £56M purpose-designed building – the Scottish Centre for Regenerative Medicine. The success of this integrated approach to neuroregeneration has led to the selection of the MRC CRM to provide the UK Regenerative Medicine Platform hub [RMP, UoA1] in "Exploiting and Engineering the Niche" (£4.5M) and a further £5M capital award from the MRC (2013) to establish a linked Centre in the Computational and Chemical Biology of the Niche, both with neural stem cell and niche biology at the core of the proposed research.

Closely associated with MRC CRM is a cluster of linked interdisciplinary research centres that capitalise on the synergies within our community so as to address key medical needs:

- ***MS Society Centre for Translational Research:*** Established in 2008 with a £2.2M award from the MS Society [led by ffrench-Constant, Chandran], brings together immunologists, neuroscientists and stem cell biologists to discover new targets for remyelination therapies. Completed a successful mid-term review in 2011;
- ***Patrick Wild Centre for Research into Autism, Fragile X Syndrome & Intellectual Disabilities*****:** Established in 2010 with £1.7M donations [led by Stanfield, Kind], this unites developmental neurobiologists & molecular medicine, including researchers in UoA11, with clinical researchers, patient families and industry (Novartis, Roche, Seaside Therapeutics);
- ***Euan MacDonald Centre for Motor Neurone Disease Research*****:** Established in 2007 with a £1M donation [led by Chandran] leading to further donations of £1.5M since 2008, it brings together neurobiologists and molecular researchers with clinician scientists and cognitive neuropsychologists;
- ***Anne Rowling Regenerative Neurology Clinic*****:** Established in 2013 following a £12.8M donation [led by Chandran, ffrench-Constant] providing a staffed 7-room clinical research facility for regenerative neurology and for the clinical study of neurodegenerative disease with a PhD & post-doctoral training programme for clinician scientists (Rowling scholarships);
- ***Muir Maxwell Epilepsy Centre:*** Established in 2012 with £1M seed funding (philanthropic plus Norwegian Research Council) [led by Chin] it brings together neurobiologists and clinical researchers at UoE with psychologists & sociologists from across Europe with the aim of translating discoveries into patient care, support in the home and community (i.e., from "*neurones to neighbourhoods*").

The MRC CRM, together with these charity and philanthropically funded research groupings, acts as a major resource and hub for the three sub-themes described below, each encompassing the clinical and non-clinical neuroscience research undertaken in these centres and also in the Wellcome Trust Clinical Research Facility (WTCRF) at the Western General Hospital, and the Edinburgh Clinical Research Facility at the Royal Infirmary of Edinburgh.

B2.1.1 Neuroregeneration (16 Cat A) (*Becker, Brophy, Chandran, ffrench-Constant, Hunt, Jarman, Kunath, Lyons, Mahad, Mason, Meijer, Pratt, Price, Sieger, Theil, A Williams)*

This group (led by Brophy) dissects the developmental genetic programmes, key transcription factors and cellular mechanisms that specify neuro-development and regeneration. The aim is to understand the pathogenesis of developmental CNS diseases, such as ciliopathies and cortical migration defects, and to develop novel regenerative strategies for MS, MND and other neurodegenerative disorders. In addition to collaborations within Edinburgh Neuroscience and Informatics (UoA11), the group has strong links with the Edinburgh MRC Centres in Inflammation Research (UoA1), and Reproductive Health (UoA1) (both have world-leading expertise in macrophage biology), reflecting the critical role of the inflammatory process in neural regeneration.

In studies pertinent to human neurodevelopmental disease, Jarman defined the gene regulatory pathways involved in ciliogenic gene expression and ciliary specialisation [**PLoS Biol 2011**, **Dev Cell 2012a**]. Pratt showed how VEGF signalling through neuroligin 1 is a critical determinant of commissural axon crossing at the optic chiasma [**Neuron 2011a**] and Price and Mason demonstrated that cortical progenitor proliferation is controlled by the transcription factor Pax6 through direct suppression of Cdk6 and hypophosphorylation of Rb [**Neuron 2013**]. Addressing the role of the oligodendrocyte, Lyons has used the power of live imaging and genetics in zebrafish to show that newly formed oligodendrocytes have only a few hours to form myelin sheaths [**Dev Cell 2013a**] and that Kif1b is essential for mRNA localisation in oligodendrocytes and the development of myelinated axons [**Nature Genet 2009**], Brophy discovered that neurofascin has a critical role in regulating action potential initiation [**Neuron 2011b**], Meijer demonstrated critical roles for Notch, HDAC1&2 and neuroregulin in the axo-glial signalling that initiates myelination [**Nature Neurosci 2009, 2011a, 2013a]** and A Williams, with Brophy, confirmed a theory proposed by Huxley in 1949 on internodal distance in myelinated nerves [**Cur Biol 2012**]. Mahad showed how glycolytic oligodendrocytes maintain myelin and long-term axonal integrity [**Nature 2012**], providing an explanation for neurodegeneration following demyelination in MS. In studies bringing together developmental and regenerative biology to identify novel regenerative strategies, ffrench-Constant and A Williams have used explant, lesion and transgenic animal models of disease to discover new targets for remyelination therapies in MS [**Nature Neurosci 2011b, 2013b**], Becker demonstrated the role of dopamine signalling in spinal cord regeneration [**Dev Cell 2013b**] and Sieger has shown that long-range Ca^{2+} waves mediate microglial migration in response to neuronal damage, a necessary step for neuronal repair [**Dev Cell 2012b**]. Finally, the development of human iPS cell models of MND by Chandran and of Parkinson's disease by Kunath led to efficient differentiation protocols and robust biomarkers of disease-related activity [**Nature Comm 2011; PNAS 2012**], paving the way for drug screening platforms and early-phase trials of cell-based therapies building on our experience of using autologous stem cells in MS [**Lancet Neurol 2012**].

The vigour and success of this research group is shown by the recruitment of a tenure-track ESAT fellow [Seiger] and 3 new chairs [Chandran, Jarman, Meijer] plus the award of a Sir David Philips BBSRC Fellowship [Lyons], a WT Intermediate Fellowship [Hunt] and 2 × £0.6M Scottish Senior Clinical Fellowships [Mahad, A Williams]. A £0.65M investment to create the WT Zebrafish Facility has substantially enhanced basic research on neuronal regeneration, in addition to a £1.75M MRC award in Optical Microscopy for Live Imaging, a £2M MS Society Centre award [ffrench-Constant, Chandran], £5M in WT programme grants [Brophy; ffrench-Constant & Brophy; Jarman], £3.1M in MRC programme grants [ffrench-Constant; Price ×2] a £1.5M MRC Efficacy & Mechanism Evaluation grant for an MS clinical trial [Chandran] and a $3M Biogen collaboration partnership for MS & MND discovery [Chandran, Lyons, ffrench-Constant, Mahad, Hardingham (B2.1.2)].

B2.1.2 Neurones & Networks (28 Cat A) (*Busch, Chin, Cousin, Daw, Dutia, Fleetwood-Walker, Garfield, Gkokgas, S Grant, Hardingham, Harmar, Holmes, Jackson, Kelly, Kind, Komiyama, Leng, Ludwig, Nolan, Oren, Osterweil, Rochefort, Shipston, Sylantyev, Torsney, van Rossum, Wyllie, Zhang)*

This group (led by Shipston) exploits imaging, electrophysiological, optogenetic, pharmacogenetic and behavioural approaches in order to understand how fundamental signalling mechanisms control synaptic function and neuronal excitability, how the resultant neural networks control defined behaviours (including feeding, motor control and cognitive tasks) and how disease-related changes lead to modified control of neural circuitry. The group aims to translate this fundamental

knowledge, through development of new animal- and human-based models, to develop rational therapeutic interventions, thereby articulating with the MRC CRM and the research within this overall theme. With strong links to Informatics (UoA11), they also develop computational predictive models to understand the properties and behaviour of neural circuits and have also been successful in establishing the joint *Centre for Brain Development & Repair* at the *Institute for Stem Cell Biology & Regenerative Medicine* (inStem) in Bangalore, India [Kind and Chandran]; this is funded by a £6M grant from the Indian Department of Biotechnology.

Since 2008, studies by S Grant and Komiyama have revealed the complexity of the genes and proteins involved in the synaptic scaffold and its relationship to vertebrate cognitive complexity through the generation and interrogation of large data sets [**Science Signaling 2009; Nature Neurosci 2008a, 2011, 2013a, 2013b; Nature 2012**]. The mechanism of synaptic function has been further elucidated by Cousin with the discovery that presynaptic GSK3 mediates phosphorylation of dynamin and controls bulk endocytosis and synaptic strength and this process is modulated by BDNF [**Nature Neurosci 2010; Nature Comm 2013**], and by Sylantyev who discovered that electrodiffusion during synaptic responses contributes to signal integration in neural circuits [**Science 2008, Neuron 2013a**], while Hardingham and Wyllie have revealed that the subtype of the GluN2 C-terminal domain of NMDA receptors, and activity-dependent regulation of antioxidant genes and mitochondrial genes, control neuronal survival [**Nature Neurosci 2008b; Neuron 2012; Nature Comm 2012a**]**.** Kind discovered that differential promoter usage and alternative splicing of SynGAP can control both the direction and magnitude of excitatory synaptic plasticity [**Nature Comm 2012b**] and that synaptic plasticity is disrupted during a critical developmental period in a mouse model of fragile X syndrome (FXS) [**Neuron 2010**], while Osterweil revealed that alterations in protein synthesis result in synaptic dysfunction in mouse models of tuberous sclerosis complex and FXS [**Nature 2011a**], and Gkogkas discovered that dysregulation of eIF4E-dependent translational control led to an imbalance in the ratio of excitatory to inhibitory synaptic inputs and autism-like phenotypes in mice [**Nature 2013**]. The channelling of synaptic information into neural networks by dendrites has been revealed by Rochefort, who has characterised the dendritic organisation of sensory input to cortical neurones *in vivo* [**Nature 2010**] while Oren has used optogenetic stimulation to discover that gamma band oscillations in the hippocampal CA3 subfield exhibit dynamical properties that are suitable for generating inter-region synchronisation [**Nature Neurosci 2012**], and Nolan and van Rossum have revealed the fine-tuning of synaptic integration in the medial entorhinal cortex into grid firing cell organisation [**Neuron 2008, 2013b**]. Investigations into the networks underlying behaviour has resulted in the discoveries by Leng that disruption of satiety signalling in the brain mediated by prolactin-releasing peptide results in obesity [**J Clin Invest 2008**] and with Ludwig that an intrinsic vasopressin system in the olfactory bulb is involved in social recognition [**Nature 2010**], the defining of the neural circuitry underlying oxygen and nutrient sensing and behaviour by Busch [**Nature 2009]**, the discovery by Zhang that potentiation of Na^+/K^+ pump activity plays an important role in determining the duration of vertebrate locomotor behaviour [**Curr Biol 2012**] and the discovery by Garfield that expression of the imprint gene *Grb10* regulates social behaviour [**Nature 2011b**].

The vigour of this group is evidenced by the recruitment of 8 new tenure-track ESAT appointments [Busch, Garfield, Gkokgas, Oren, Osterweil, Rochefort, Sylantyev, Zhang], the appointment of 6 new chairs [Cousin, Dutia, Hardingham, Kind, Ludwig, Wyllie], 4 fellowships [Hardingham (MRC SRF), Nolan (Marie Curie), Rochefort (WT Sir Henry Dale, awarded 2013), Torsney (RSE-Caledonian)], over £3.4M in UK funding, including 3 programme grants [Shipston ×2 (WT and MRC), Wyllie (MRC, co-PI)], and €9.99M in EU funding, including EU FP7 funding for GENCODY, EUROSPIN and SYNSYS [all S Grant], Consortia EU funding as PI and co-PI with multiple European partners and SME's to Leng (including EUFP7: Full4Health [with Shipston], EC diabesity and EC Neurofast) investigating the neurobiological basis & gut–brain interactions involved in the decision to eat. In addition, S Grant is also Co-Director for Molecular and Cellular Neuroscience on the €1 billion Human Brain Project (€1.1M already awarded for ramp-up phase), with Chandran (this UoA) and Armstrong (Informatics, UoA11). This sub-theme has also established the Muir Maxwell Epilepsy Centre [Chin, see B2.1], co-established the Patrick Wild Centre [Kind, see B2.1 & B2.2.3] and attracted major philanthropic donations to support *in vivo* (multiphoton) imaging (Shirley Foundation, £1M).

B2.1.3 Degeneration (23 Cat A, 2 Cat C*) *(Abrahams, Al-Shahi Salman, Andrews*, Bak, Deighton, Della Sala, Dennis, Fleck*, Gillingwater, Green, Horsburgh, Ironside, Knight, MacLeod, MacPherson, Marshall, Parra, Ribchester, Sandercock, Smith, Spires-Jones, Sudlow, Wardlaw, Whiteley, Will)*

This sub-theme brings together clinical and basic neuroscientists (led by Sandercock) with cognitive neuropsychologists (led by Della Sala) to understand the causes, consequences and mechanisms underlying degeneration, whether from primary diseases of neurones and glia (e.g., MND or dementia) or secondary to vascular disease (e.g., stroke and vascular cognitive impairment) or trauma, and translate these into methods for diagnosis, prevention and treatment.

Using animal models of neurodegenerative disease, Spires-Jones discovered that despite the slow nature of progression of Alzheimer's disease, the two hallmark pathologies, plaques [**Nature 2008**] and tangles [**Nature 2010**] form remarkably rapidly, and that pathological forms of tau spread through neural circuits [**Neuron 2012**] explaining the stereotypical march of the disease through the brain, while Gillingwater revealed selective vulnerability of motor neurones conforming to a fast synapsing phenotype in a model of spinal muscular atrophy [**Hum Mol Genet 2008**]. Neuropathology by Green, Ironside, Knight and Will identified transmission routes, risk factors, biomarkers and established diagnostic criteria for CJD [**J Neurol 2009; J Gen Viol 2009, 2011; PNAS 2010**]. Working with Alzheimer's disease patient cohorts, Parra, Della Sala and Abrahams discovered short-term memory binding deficits that can predict disease before other symptoms appear [**Brain 2009, 2010**], while Della Sala has developed a cognitive marker for the disease [**J Neurol 2009**].

This group has also addressed the urgent need for effective therapies for ischaemic and haemorrhagic stroke. With advanced human imaging technologies to study pathogenesis of stroke and cognitive decline, Munoz Maniega and Wardlaw have shown the role of blood brain barrier failure in lacunar stroke and cerebral small vessel disease [**Ann Neurol 2009**]. Sandercock, Wardlaw and Dennis have led major international multi-centre trials that have significantly altered clinical practice; the IST-3 trial and meta-analysis showed thrombolysis treatment for stroke benefits a much wider variety of patients and indicated for the first time benefit in patients aged > 80 [**Lancet 2012a, 2012b; Lancet Neurol 2013**] while the CLOTS-1, 2 & 3 trials defined optimum physical methods for DVT prevention after stroke [**Lancet 2009, 2013; Ann Int Med 2010**]. Al-Shahi Salman has led a programme of research on the prognosis, prevention and treatment of haemorrhagic stroke [**Lancet 2012c**; **Lancet Neurol 2008, 2012**]. Sandercock has played a major role in the CRASH-2 large-scale clinical trials in trauma [**Lancet 2010]**, and collaborated on EUROTHERM, the international randomised trial led by Andrews* (ongoing). In further work on trauma, Andrews* has found that selenium reduces infections in critically ill patients [**BMJ 2011**] while Fleck's* work on the BOOST II trials has helped define safe oxygen saturation levels for preterm infants [**New Eng J Med 2013**]. Building on Sandercock's international expertise in clinical trials, research evidence synthesis and meta-analysis, MacLeod applied these techniques to preclinical science to identify why almost no candidate drugs from animal studies have shown benefit in clinical trials. Macleod demonstrated publication bias [**PLoS Biol 2010**] and excess significance in the *in vivo* literature due to non-reporting of negative findings [**PLoS Biol 2013**], leading to the adoption of his CAMARADES Group's risk of bias methods in Landis Transparency recommendations (*Nature*, 2012, 490:187-91).

The strategic importance of this sub-theme is highlighted by the award in 2012 of an MRC Mouse Consortium Network "*nPAD" Neurodegenerative Processes of Aging and Disease*", which will provide access to novel mouse models [Manson (UoA6) lead PI with 21 co-PIs from this UoA] and the philanthropic investment of a further £1.5M since 2008 into the Euan MacDonald Centre for MND Research, a platform for translational interdisciplinary research such as the voice-banking project, a collaboration between neuroscience, informatics and linguistics in which voices of MND patients are stored digitally so that reconstruction by computer later in the disease preserves the unique features of that individual. The major influence on research and clinical imaging of this group, which we expect to have major impact over the next 5 years, is emphasised by 1) MRC, DZNE (German Funding Council) and Canadian Institutes of Health Research funding for Centres of Excellence in Neurodegeneration (COEN) to define imaging standards for small vessel disease as laid out in an influential position paper [Wardlaw, *Lancet Neurol*, 2013,12:822-38]; 2) two major reports on the ethical, legal and management aspects of incidental findings in research imaging;

and 3) €10M FP-7 funding for the EUROHYP-1 trial, capitalising on expertise in brain cooling and in clinical trials [MacLeod].

The vigour of this sub-theme is evidenced by the appointment of a tenure-track ESAT fellow [Spires-Jones], the award of an MRC Senior Clinical Fellowship [Al-Shahi Salman], MRC Clinician Scientist Fellowship [Whiteley], an Alzheimer Society Fellowship [Parra] plus a Stroke Association Princess Margaret Award to establish a clinical academic training programme in stroke [Whiteley] and 5 new chairs [Gillingwater, Horsburgh, MacLeod, Al-Shahi Salman, Sudlow].

B2.2. Healthy & Impaired Cognition & Behaviour Across the Lifespan

Research by the 56 Cat A and 4 Cat C staff in this theme spans healthy cognition and behaviour, and disorders of the individual across the lifespan, including autism and schizophrenia. The MRC Centre for Cognitive Ageing & Cognitive Epidemiology is a major nucleus. Research covers three sub-themes: (1) Individual Differences in Cognition, (2) Language, Memory & Perception and (3) Psychiatric Disorders across the Lifespan.

The MRC Centre for Cognitive Ageing and Cognitive Epidemiology [Director, Deary; 2008: £3.4M from MRC; in 2013: £3.5M from the MRC] brings together one of the largest concentrations of experts on the psychology of individual differences with world-class imagers, human experimental cognitive psychologists, human and animal behavioural researchers, as well as geneticists in the MRC Institute for Genetics & Molecular Medicine (IGMM) (UoA1). This has resulted in an exceptionally productive series of cross-disciplinary collaborations, attracting additional external grant awards of over £15M. The MRC CCACE has also resulted in greater integration within Psychology since RAE2008, with joint grants, publications and PhD supervision established between the 2008 themes of Human Cognitive Neuroscience and Individual Differences. Housed in the same refurbished building that hosts MRC CCACE core activity, as well as research on Language, Memory & Perception, is the sister Alzheimer Scotland Dementia Research Centre. The latter is focused on developing a brain bank (in collaboration with the Edinburgh Sudden Death Brain Bank [Smith]) and supporting access to dementia patients for research studies through the Scottish Dementia Research Network [Director, Starr]. Crucially, MRC CCACE provides administrative staff (scientific and clerical) and research infrastructure staff (statistics, database management, genetics, animal and human testing technicians and knowledge exchange) that allow the Centre to act both as a major research generator and a major research hub for the sub-themes below.

B2.2.1 Individual Differences in Cognition **(16 Cat A, 1 Cat C*)** *(Bastin, Bates, Booth, Deary, Gale, Johnson, Luciano, MacLullich, Marioni, Möttus, Munoz Maniega, B Roberts (nee Shipley), N Roberts, Shenkin, Starr*, Weiss, Yau)*

This sub-theme (led by Deary) examines the nature, determinants, consequences and mechanisms of individual cognitive abilities and cognitive changes across the life course. Since 2008 this group has also established and led the field of cognitive epidemiology, studying populations to understand the mechanisms of associations between cognition and later health inequalities. To achieve these dual aims, the group is expert in animal studies, large human cohort studies such as the Lothian Birth Cohorts of 1921 (LBC1921) and 1936 (LBC1936), the longest follow-up studies of cognition in the world, and international genome-wide association study (GWAS) consortia of cognitive and brain phenotypes, e.g., the CHARGE and ENIGMA consortium meta-analysis studies.

With respect to cognitive differences between individuals, Johnson showed that the general cognitive factor is almost invariant between test batteries [**Intelligence 2008**]. In a number of pioneering studies on cognitive genetics, Deary was the first to show from DNA testing (GWAS) that human intelligence is highly heritable and polygenic [**Mol Psychiat 2011**], and discovered that genetic variation contributed about a quarter of the causes of change in cognitive ability between childhood and old age, that many of the same genes contribute to cognitive ability in childhood and old age, and that the *APOE* locus is implicated in nonpathological cognitive ageing [**Nature 2012**; **Mol Psychiat 2012a**]**.** Munoz Maniega discovered that white matter integrity is a general property of distributed brain regions in old age and a foundation of processing speed and general cognitive ability in older age [**Mol Psychiat 2012b**], while Bastin revealed that the association between cognitive ability and cortical thickness in old age is predicted by childhood mental ability [**Mol**

Psychiat 2013a] and Booth showed that the integrity of brain white matter in older people is associated with their extent of independent living in the community [**Neuropsychol 2013**]. Bates showed an association between language abilities and a mutation in DYX1C1 [**Mol Psychiat 2010**]. In cognitive ageing, Luciano conducted the first GWAS of processing speed [**Biol Psychol 2011**], while Marioni's large-scale research established associations between markers of inflammation and cognition in old age [**Psychosom Med 2009a; Diabetes 2010**]. Luciano crucially discovered 'reverse causation' in associations between inflammation and cognitive ageing [e.g., **Psychosom Med 2009b**] while in a GWAS, Starr* found that APOE may be involved in cognitive ageing [**Mol Psychiat 2013b**]. Animal studies by Yau discovered the pivotal role played by local brain amplification of glucocorticoids by 11β-hydroxysteroid dehydrogenase type 1 in age-related memory deficits [**J Neurosci 2010a, 2010b, 2011**], confirmed by MacLullich in humans [**Neurobiol Ageing 2012**].

In cognitive epidemiology, Gale found novel associations between cognitive ability, mental disorders and health behaviours in youth and mental and physical disorder in later life [**Arch Gen Psychiat 2008, 2012; Arch Int Med 2010].** She discovered that people high and low in cognitive ability in early life are more prone to bipolar disorder [**Mol Psychiat 2013c**]. B Roberts used large-scale longitudinal data to discover the associations between cognition and specific causes of death [**J Psychosom Res 2008**]. Möttus showed that health literacy is not a key determinant of health in older people, because it is largely confounded by childhood intelligence [**Health Psychol 2013**], and conducted one of the first large longitudinal studies of the stability and change of personality in old age [**Psychol Aging 2012**]. He also led a collaboration across 20 countries showing how response style can influence self-reports of personality traits [**Personal Soc Psychol Bull 2012**]**.** MacLullich showed that delirium is a strong risk factor for dementia in the oldest old [**Brain 2012**], Bates discovered a genetic overlap between neuroticism and schizotypy [**Behav Genetics 2012**] and Weiss found the genetic link between personality traits and wellbeing [**Psychol Sci 2008**], also revealing that primates experience a mid-life crisis [**PNAS 2012**].

The strategic importance of this sub-theme is highlighted by the creation, in 2011, of the Alzheimer Scotland Dementia Research Centre [led by Starr] with £0.75M core-funding from Alzheimer Scotland, which will work closely with the Edinburgh Sudden Death Brain Bank [led by Smith, B2.1.3] and MRC CCACE.

The vigour of this group is evidenced by the recent recruitment of 4 tenure-track ESAT researchers [Booth, Luciano, Marioni, Möttus], a reader in cognitive epidemiology [Gale], the award of an Alzheimer Society Fellowship in this REF period [Marioni], a chair [MacLullich], a new clinical senior lecturer [Shenkin] and a $3.4M grant from the NIH for a twins study looking at alcoholism in females [Johnston, 2010–2014]. The Lothian Birth Cohort Studies have attracted £7M in core support from Age UK since 2004, with additional funding from the BBSRC and MRC.

B2.2.2. Language, Memory & Perception (28 Cat A, 1 Cat C*) *(Auyeung, Branigan, Carmel, Chevalier, Corley, Cowan, Doumas, Engle, Gherri, Hardt, Logie, Martin, R McIntosh, McKinlay, Moore, Morcom, Morey, Morris, Nieuwland, Nonaka*, Nuthmann, Pickering, Rabagliati, Shillcock, Simner, Sturt, Wang, J Williams, Wood.)*

This sub-theme brings together research with healthy human participants (led by Logie) with that in animal models (led by Morris) to understand cognition and behaviour across the lifespan. Human research is housed in the newly built and refurbished laboratories for Cognitive Neuroscience and uses cognitive and behavioural experimental techniques, communication and discourse analysis, eye tracking, transcranial magnetic stimulation, conceptual and computational modelling, and functional brain imaging (two parallel EEG/ERP systems in house, and fMRI at the Brain Research Imaging Centre), to understand language processing in monolingual and bilingual adults, language development in infancy, working memory, visual perception and links between perception and action control. In adjacent laboratory space, the study of neurobiological mechanisms of memory in animal models uses behavioural, electrophysiological and state-of-the-science optogenetic systems. Researchers within the sub-theme have strong links with Linguistics (UoA 28) and Informatics (UoA11). There are joint grants and co-supervised PhD students with researchers from the Individual Differences in Cognition sub-theme [B2.2.1, Deary, Johnson] and with the Neurodegeneration sub-theme [B2.1.3, Abrahams, Della Sala, Parra].

During the REF period, new animal behavioural studies by Morris on schemas have been the first to show parallel encoding of new episodic memory traces in neocortex during hippocampal-dependent learning [**Science 2011**], triggering a major revision of Jay McClelland's (USA) influential "complementary learning systems" hypothesis. Morris and Nonaka* furthered understanding of the neural mechanisms underlying their synaptic-tagging and capture theory [**PNAS 2010; Cell 2012; Nature Comm 2012**]**.** Hardt discovered that PKMzeta maintains memories by regulating GluR2-dependent AMPA receptor trafficking [**Nature Neurosci 2010**]. In human behavioural research, Pickering made major theoretical advances in understanding how language production and comprehension are integrated, with interlocutors constructing and imitating forward models in dialogue [**Behav & Brain Sci 2013**], complementing Branigan's discovery of co-activation of syntax in bilingual language production [**Cog Psychol 2011**]. Cowan and Della Sala demonstrated the role of interference in dense amnesia and how minimising interference might have therapeutic benefits for both healthy older people and amnesic patients [**Psychol Sci 2012**]. Morcom's work offered new insight into modular reorganisation in functional brain networks with age [**Neuroimage 2009**], and Logie's study with Johnson, involving over 90,000 participants internationally, revealed how different cognitive abilities are differentially affected by age, as well as demonstrating that older and younger people perform the same cognitive tasks in different ways, questioning widespread assumptions of measurement invariance in lifespan psychometric testing [**Intelligence 2010**]. Engle's demonstration that some claims for the generalised benefits for working memory training are ill-founded [**JEP: General, 2013**] is a major systematic contribution to a debate that often confounds scientific advance with commercial and ideological pressures. In research on visual perception, Nuthmann made a major theoretical advance in computational modelling of the complex and often intractable area of dynamic scene perception [**Psychol Rev 2010**], while Carmel [**J Vision 2008**] used new rigorous methodologies to show how perceptual load impacts on non-conscious orientation of attention. Auyeung demonstrated that levels of testosterone in the foetus predict the presence of autism in young children and have differential effects across genders [**Br J Psychol 2009; Psychol Sci 2009**]. Cowan [**Psychol Rev 2012**], Engle [**JEP: Learn Mem Cog 2013**] and Logie [**J Mem Lang 2008; Mem Cog 2011**] made important contributions to the debate concerning the functional organisation and capacity limitations of working memory, and Moore was among the first to report a clear demonstration of the neural generators for domain-general working memory function [**Neuroimage 2011**]. Theoretical work by R McIntosh advanced understanding of mapping of perception and action onto parallel but interacting neural generators [**Cog Neurosci 2010]**.

The vigour of this group is highlighted by the recent appointment of 11 high-quality tenure-track ESAT researchers [Auyeung, Carmel, Chevalier, Doumas, Hardt, Martin, Moore, Morey, Nieuwland, Nuthmann, Rabagliati], a Caledonia Research Foundation Royal Society of Edinburgh fellowship [Wang], an EU Marie Curie Research Fellowship [J Williams], the appointment of 2 part-time professors [Cowan and Engle], both experts in areas of working memory to continue collaborative work with Della Sala and to develop new research collaborations within and across themes, and by £4.5M current grant funding including an ERC Advanced Investigator Grant to Morris (2011–2016), a £1.2M HFSP grant investigating decision-making in rats [Wood, joint PI], an FP7 Large Scale Integrating Project grant to Logie (2013–2015) who is the only cognitive psychologist among 10 commercial and academic information technology partners across 7 EU countries, and a prestigious ESRC 'Future Research Leader' research grant to a new young member of staff, Martin, to develop her research on sentence-processing using behavioural and ERP techniques.

B2.2.3 Psychiatric Disorders (12 Cat A, 2 Cat C*) *(Chan, Eiroa-Orosa, Ferreira, R Grant*, Hutton, Lawrie, Lwin, A McIntosh, Owens, Schwannauer, Stanfield, Stone*, Sussmann, Whalley)*
This group of psychiatrists (led by Lawrie) and clinical psychologists (led by Schwannauer) aims to understand the mechanisms that underlie psychiatric illness and emotional well-being from childhood to adulthood, including the psychological impact of chronic physical ill health. This lifespan approach articulates extremely well with the research within CCACE and the overall theme of healthy and impaired cognition and behaviour. This group works with colleagues across Edinburgh Neuroscience employing technologies including iPS cells, genetics and neuroimaging as well as clinical trials.

Since 2008 this group has published widely on four separate prospective longitudinal studies of cohorts at high risk and first onset of psychosis, e.g., A McIntosh showed that increased risk of bipolar disorder is associated with abnormal white matter integrity and neural function [**Biol Psychiat 2011a, 2011b**], Stanfield found that that an increased risk of schizophrenia in young people who have intellectual impairment is associated with both cortical folding anomalies and grey matter changes [**Biol Psychiat 2008, 2013a**] and Lawrie & Owens discovered that a genetic high risk of schizophrenia is associated with changes in cortical volume that correlate with increasing severity of psychotic symptoms [**Biol Psychiatry 2011c**]. A McIntosh also found that the psychosis susceptibility gene neuregulin 1 is associated with reduced white matter density and integrity in human subjects [**Mol Psychiat 2008**] and, using GWAS, found that increased polygenic risk of schizophrenia is associated with lower cognitive ability at age 70 [**Biol Psychiat 2013b**]. In our clinics R Grant* found that 20% of patients with gliomas develop clinical depression within 6 months [**J Clin Oncol 2011**] and Stone* characterised functional symptoms unexplained by disease [**Brain 2009, 2010**]. Working with bipolar disorder and psychosis patients, Schwannauer and Chan developed psychological models of, and determined key vulnerability factors in, the development of complex mental health problems, crucial to place effective clinical interventions earlier in the care pathway and develop effective health promotion strategies [**Br J Psychiat 2009; Schiz Bull 2013**], while Hutton established that cognitive behavioral therapy could be a suitable treatment for schizophrenia patients not on antipsychotic medication [**Psychol Med 2012**].

The vigour of this group is evidenced by the strategic appointment of 4 tenure-track ESAT researchers [Chan, Eiroa-Orosa, Ferreira, Hutton] the award of 3 clinical fellowships [McIntosh (Scottish Senior CRF), Stanfield, Sussmann (both WT CRF's)], a non-clinical fellowship [Whalley, Dorothy Hodgkin] and two chairs [McIntosh, Schwannauer], the award of over £2.7M in grant funding including >£1.5M funding for stem cell research [McIntosh], £0.8M as part of EU brain imaging consortia [Lawrie, McIntosh], a £1M Pfizer Neuroscience Grand Challenge award for human brain imaging, the award of £0.4M to investigate Cognitive Behaviour Therapy for Clozapine-Resistant Schizophrenia [Schwannauer] and £0.5M for the Sackler Centre for Developmental Psychobiology. A further £0.7M donation created, in 2010, the cross-disciplinary *Patrick Wild Centre* [see B2.1, co-led by Stanfield, Kind], which is currently the UK coordinator for the Roche clinical trial for FXS, and also participating in trials by Novartis & Seaside Therapeutics. In 2011 the commitment to high-quality training in psychiatry was reinforced with the award of the £2.15M Medical Research Foundation (the MRC research charity) postgraduate psychiatry training scheme ('PsySTAR', profiled in *Lancet* 2011, 36: 61679-6), led by Lawrie.

B3: Overarching Future Aims (2014–2019)

In the REF2014 period, we have focussed around 2 major themes and have substantially expanded our research staff and capabilities. However, Edinburgh Neuroscience remains an "Institute without walls", currently occupying 8 buildings. In the next 6 years, we have advanced plans to rectify this, without jeopardising key connections among complementary experts, patients and our healthy ageing cohorts. We will further grow capacity and drive attainment in our major areas.

An Institute with walls.

We will focus all basic and clinical neuroscience on our main new Royal Infirmary campus at Little France, with Psychology expanding in the central area adjacent to Informatics and Linguistics, but with 'hot desk' and experimental facilities at our multimodal human imaging centre at the Royal Infirmary. Thus, all clinician- and basic scientists working in neurodegeneration, stroke, neurones & networks and on imaging components of human cognition will coalesce in new buildings adjacent to ongoing developments in stem cell biology, inflammation, bioengineering and imaging on the Little France campus. The infrastructure will be provided by a new £50M research building adjoining (and linked to) the new MRC CRM. NHS Lothian is currently constructing the clinical neurosciences hospital on this campus (opening 2017).

The interdisciplinary environment for research into cognition and behaviour across the lifespan and MRC CCACE will remain focussed at the George Square campus, 15 minutes from Little France (free shuttle bus), to ensure that these researchers benefit from strong interactions with neighbouring developments in Linguistics (UoA 28) and Informatics (UoA 11). Clinical psychology

will be provided with dedicated laboratory space in a newly refurbished building and we will expand the Cognitive Neuroscience Laboratory to incorporate EEG and Near Infra-Red Spectroscopy for research with human infants, with new build and further major refurbishment of the existing Psychology building coupled with £5M University investment in the MRC CCACE to 2018.

Next-generation imaging.
We will consolidate all major *in vivo* research imaging technologies at Little France under the umbrella of 'Edinburgh Imaging'. We will expand facilities to include an *in vivo* animal imaging facility for the entire neuroscience community, designed for long-term experiments using existing and new confocal, multi-photon and super-resolution optical imaging alongside 7T MR and CT-PET. A further research-dedicated human MR imaging suite will be opened close to NHS Accident & Emergency, providing a 'hot' imaging facility for research into the earliest, hyperacute effects of stroke, inflammation, ageing and the neurological consequences of systemic disease, whilst the £20M Clinical Research Imaging Centre (CRIC; Deputy Director, N Roberts) (3TMRI and 320 slice CT) at Little France will continue to support functional and structural imaging of the healthy and ageing brain.

Cutting-edge research technologies.
We will drive ever closer and deeper links with informatics, exploiting the Scottish node of the MRC-funded and University of Dundee-led Farr Institute, which is based at the Royal Infirmary campus, and Scotland's coordinated electronic records and health system. We will use this to devise novel methodologies for deep phenotyping of healthy subjects, young and elderly, and of patients, for instance with MS or MND, to stratify and drive experimental medicine and early-phase trials on novel regenerative therapies. Edinburgh Genomics has the UK's second-highest capacity for sequencing and we will increasingly stratify cohorts for study to the finest degree. We will drive fundamental psychology and brain sciences, linking with Linguistics, Imaging, Engineering and Chemistry to devise a host of novel tools to interrogate the normal and disordered brain.

C. People, including:

C1: Staffing strategy and staff development

The principal strength of Edinburgh Neuroscience lies in its scientists, and the highly collaborative research environment in which they work. In order to increase leadership and ensure succession there has been focussed and strategic appointment of 19 new chairs, including the Directors of the MRC CRM [ffrench-Constant] and of the Euan MacDonald Centre for MND Research and Anne Rowling Regenerative Neurology Clinic [Chandran]. To expand research capacity and further encourage interdisciplinary activity, we have strategically recruited 29 outstanding **Edinburgh Scientific Academic Track** (ESAT) researchers. Moreover, the University is making a further 50 new 5-year ESAT positions available across UoE in 2014. These prestigious posts, which include UoE Chancellor's Fellowship positions, are anticipated to lead to permanent senior posts. This is part of our mission, outside REF, to be the UK's leading institution supporting the development of early career academic staff, reinforced by our 30-FTE Institute for Academic Development (www.ed.ac.uk/schools-departments/institute-academic-development). Coupled with the retention and career development of our most promising early years investigators (18 externally funded fellowships since 2008, 7 of them clinical), this has generated a stimulating, creative and highly successful environment as evidenced by the spread of fellowships between development, clinical and senior staff [Al-Shahi Salman, Hardingham, Hunt, Jackson, Lyons, Mahad, A McIntosh, Morcom, Nolan, Nuthmann, Parra, Rochefort, Stanfield, Sussmann, Theil, Torsney, Whalley, A Williams]. Clinical academics are appointed to a 50:50 NHS:UoE contract, but with extra academic activity funded by UoE, to facilitate research momentum in the face of busy NHS responsibilities.

A key part of our successful career development strategy has been the implementation of the concordat for Career Development of Researchers, ensuring that staff are appraised annually and given guidance on career development, for which the University was awarded the HR Excellence in Research Award in 2010 by the EC. Our Institute for Academic Development provides a wide range of career and professional development support specifically for research staff, transferable skills training, a mentorship scheme, leadership and management training. All new tenure track staff are given the opportunity to be involved in co-supervision of PhD students, together with an experienced staff member. The university also provides expert support for staff grant applications

and grant administration, through Edinburgh Research and Innovation, as well as discipline-specific research administrative support in each sub-theme. Edinburgh Neuroscience offers internal peer-review support for all research grant preparation. Further staff support is provided by University competitive funds for pilot studies (e.g., Challenge Investment Fund), and there are funds for staff to present their research at conferences, to host short visits by leading researchers from elsewhere, and all research active staff are eligible to apply for one semester of research leave after completing six semesters of their full teaching and administrative duties.

Equality and diversity is also embedded in University practice: it has been a member of the Athena Swan Charter since 2005, was awarded a Bronze Award in 2006, and renewed in 2009 & 2013. Furthermore the School of Biomedical Sciences (which hosts much of Edinburgh Neuroscience) received a Silver Award in 2011 while Psychology and Clinical Psychology are currently submitting for Bronze Awards. Within this UoA return, 32% of researchers are female and 29% are from other countries (an increase from 29% and 12% respectively in RAE2008). The University established a Lesbian, Gay, Bisexual & Transgender Staff Network in 2012, enabling the involvement of LGBT staff in the development of University policies, promoting an inclusive working environment and bringing together staff with common research interests.

C2: Research students

Edinburgh Neuroscience provides a supportive and nurturing environment for early years researchers and students, reflected in an increase in the number of students completing PhDs (in REF period, a total of 192 doctoral degrees were awarded; increasing from 30 in 2008/9 to 48 & 41 in 2011/12 & 2012/13 respectively). In addition to University- and individually funded PhD places we have innovative, cross-disciplinary and cross-institution MSc & PhD training programmes:

- MSc by Research in Integrative Neuroscience combines with first year of Neuroinformatics Doctoral Training Centre (UoA11) to provide joint training for MSc and doctoral students
- MRC funded CCACE 1 plus 3 (MSc + PhD) programme (2 per year since 2009)
- ESRC Doctoral Training Centre pathways for Psychology and for Language Sciences in the Scottish Graduate School of Social Science (co-lead, Corley) (5 per year to Edinburgh)
- PsySTAR postgraduate psychiatry training scheme (Director, Lawrie), initiated with £2.15M funding from the MRC/MRF, is led by UoE on behalf of 4 Scottish universities, modelled on the ECAT scheme (9 studentships over 7 years; profiled in *Lancet*, 2011, 378:1911)
- ECAT interdisciplinary lectureship programme offering PhD and postdoctoral/lectureship support to clinicians wanting to become researchers, underpinned by a £6.2M award from WT (5 clinical PhD students per year; 20% undertake neuroscience projects)
- Scottish Imaging Network – A Platform for Scientific Excellent (SINAPSE, funded by Scottish Funding Council & the Chief Scientist Office) 4-year PhD programme
- Rowling fellowship scheme – clinician scientist 3-year PhD programme in regenerative neurology (1 per year since 2012)
- NHS for Education Scotland-funded three year Doctorate in Clinical Psychology programme and 1-year MSc in Applied Psychology for Children and Young People
- Joint PhD programme between UoE and Suor Orsola Benincasa University, Naples; students spend time in both Universities and the PhD is awarded by both Institutions

In line with University policy, each PhD student has a primary and secondary supervisor and, since the ethos of Edinburgh Neuroscience is interdisciplinary activity, collaborative projects are strongly encouraged. All supervisors are required to attend regular training sessions. Student progress is assessed by a thesis committee, which includes the supervisors and at least two advisors one of whom must be outside of the supervision team. Students also have access to the Institute for Academic Development for transferable and scientific skills training as outlined in the Vitae Researcher Development Framework. Postgraduate committees within the administrative Schools oversee training quality and pastoral support. In addition:

- The Scottish Universities Psychology Postgraduate Research Training (SUPPORT) network organises specialist research training days for research postgraduates in Scottish University

Psychology departments;

- The Edinburgh Neuroscience Autumn School for PhD Students (established 2012, 50 students per year from all backgrounds) provides tailored neuroscience-related career development training. Delivered by Edinburgh Neuroscience researchers, it is designed to encourage interdisciplinary mixing from the first stages of a research career;
- Students and early years researchers are proactively nominated for awards, e.g., in 2011 the inaugural Royal Society of Edinburgh Beltane Innovators Award for Public Engagement was awarded to Joanna Brooks, a PhD student in Psychology [Della Sala/Logie], and in 2012 the British Neuroscience Association Undergraduate Award was presented to Lewis Hou, a final year BSc (Hons) student);
- Postgraduate students are encouraged to participate in the broad public engagement programme run by Edinburgh Neuroscience, from schools workshops (4165 pupils since 2008) to events for adults (6571 in REF period) and Science Festivals (33,000 people), providing them with opportunities for training and hands-on experience.

Edinburgh Neuroscience is committed to further expanding the training of young clinician scientists, building on our successful models in i) regenerative neurology (Rowling scholarships), ii) a fully funded PhD programme integrated into clinical training (WT-ECAT). We will also take additional advantage of funding schemes (e.g., Experimental Psychology Society, Physiological Society, Psychonomic Society) for non-clinical PhD students to study for short periods in other world-class research centres.

D. Income, infrastructure and facilities

D.1. Income

Since 2008 Edinburgh Neuroscience has expanded its income stream from both research councils and philanthropic sources, as a result of which income has increased to a current total grant portfolio spend of £90.4M. Details of larger individual grants have been included within the sub-themes in section B2.

D.2. Infrastructure and Facilities

We have won substantial infrastructure investment since 2008:

£56M (from a combination of University funds and support from the Scottish Government, the EU, the MRC and the BHF) has been **invested in the Scottish Centre for Regenerative Medicine** (opened 2012) that houses the work of the MRC CRM on neuroregeneration and disease modelling using iPS cells, and includes a £20M GMP facility for generating ES and iPS-derived products for clinical use.

A private donation of £12.8M led to the **establishment of the new Anne Rowling Regenerative Neurology Clinic** (opened 2013), a patient-oriented initiative underpinned by laboratory and clinical research into neurodegenerative conditions such as MS and MND and whose clinical trials expertise will be maximised by the WTCRF; hub of the Edinburgh Clinical Trials Unit and ACCORD (Academic & Clinical Centre Office for Research & Development).

Infrastructure investment (£17M) for new build and major refurbishment of two neighbouring buildings has **created an integrated academic environment spanning Psychology, Linguistics, Philosophy and Systems Neuroscience** with state-of-the-science behavioural, electrophysiological and optical imaging facilities for animal studies, and for human studies, a new cognitive neuroscience laboratory suite comprising two 128-channel EEG/ERP systems with dedicated eyetrackers, transcranial magnetic stimulation, direct current stimulation, and Optotrak infrared motion capture system and eyetracker, in addition to over 40 general purpose bookable laboratory rooms with networked computers, audio recording studios with four acoustically isolated rooms, a near-anechoic chamber for very high-quality low-reverberation voice recording, two further eyetracker laboratories and a further new laboratory suite with dedicated eyetracking for the study of human infant language and perception.

Strategic investment (2008–13) in imaging facilities to support the future strategy of using animals

and human research as parallel and synergistic approaches includes:

- The Brain Research Imaging Centre led by Wardlaw supported our studies using MR scanning on stroke and structural changes associated with psychosis, ageing and cognitive decline;
- The WT £20M CRIC at Little France additionally provides 320 slice CT, CT/PET (with a GMP-compliant cyclotron) as well as 3T-MRI;
- Optical imaging has been supported by an MRC award in Optical Microscopy (£1.75M) for an *in vivo* imaging facility, using spinning disk and multi-photon microscopy, and the construction of the WT Zebrafish Facility & Optical Microscopy Unit, both at Little France;
- Little France houses one of the largest modern animal units in Europe, incorporating multimodal animal imaging and behavioural testing suites, with 7T-MRI, Intravascular Ultrasound (IVUS) and other *in vivo* optical imaging, rodent ultrasound, behavioural testing suites and telemetric monitoring of multiple physiological modalities;
- A £1M Shirley Foundation donation provided two bespoke machines for the multiphoton confocal facility;
- The MRC Centre for Regenerative Medicine has, as part of its successful renewal in 2013, received funding to develop super-resolution microscopy on the Little France campus in collaboration with the MRC-funded Edinburgh Super-resolution Imaging Consortium based at Heriot Watt University (a £1.5M total investment).

In addition to a dedicated scientific administrator for Edinburgh Neuroscience, in this REF period we have appointed an additional scientific administrator, statistical and genetics support staff, a brain imaging development officer, human testing officer, animal testing technician, a knowledge exchange officer, five senior-grade research MR and ultrasound radiographers, a scientific business manager, four research administrators, an image data manager, two medical physicists, two image analysis software developers, three clinical trials image managers, two image analysts, a statistician and a web developer/knowledge transfer officer, as well as several honorary academic consultant level neuroradiologists and 8 computing technical support staff.

E. Collaboration or contribution to the discipline or research base

E1. Collaboration

Researchers are involved in a large number of collaborations, both nationally and internationally. Some have been outlined above (B), but examples of broader programmes include:

- National Centre for Biological Sciences (NCBS), Bangalore and International Stem Cell Institute, Bangalore (InSTEM). Involving members of the Patrick Wild Centre, this partnership focuses on FXS, autism and disorders of the synapse. £6M funding has been secured from the Indian Government (see B2.1.2);
- Brain Centre Rudolf Magnus, UMC, Utrecht. A cross-disciplinary partnership involving members of the Degeneration/Regeneration, Neuronal Networks, Stroke, Neurodevelopmental Disorders and Psychosis research groupings. This has resulted in a €60,000 grant for joint activities and several joint publications and research grants;
- Queensland Brain Institute (QBI), University of Queensland, Brisbane. This is a formal partnership between Deary's cognitive genetics group in Edinburgh and Peter Visscher's Quantitative Genetics group at the University of Queensland. This has resulted in, for example, papers in Nature, Science and Molecular Psychiatry. QBI contributes funds toward genetic testing in Deary's birth cohorts and part of the salary of one of the new ESAT Fellows;
- Scottish Imaging Network: A Platform for Scientific Excellence (SINAPSE). A network of 6 Scottish Universities, bringing together international expertise in imaging to create a shared environment for strategic research, education and knowledge transfer. Established in 2007 with £7.4M funding from the Scottish Funding Council and the Chief Scientist Office, this network continues to provide direct access to outstanding imaging expertise and offers a programme of joint PhD students [Wardlaw, Director 2007–2011].

E2. Contribution to the Discipline

***Membership of Grant Review Groups and Panels*:** At least 22 of our researchers sit on 32 grant awarding panels, from charities to national and international funding bodies, including: **BBSRC:** Fleetwood-Walker (Scientific Steering Group for Capacity Building Awards); **MRC:** Chandran (current), Deary (current), Hardingham (current), Knight (current); **WT:** ffrench-Constant (Panel Chair, current), Morris (Head of Neuroscience 2007–2010), Wyllie (2008–11); **Joint UK Research Councils**: Starr (Life Long Health & Well Being Board 2008–11); **European Research Council:** Lawrie (Neurosciences panel 2012), Logie (Advanced Grants panel, deputy chair since 2009]; **European Commission:** S Grant (Peer Review Panel, current)

Contribution to Societies and Organisations: 22 of our researchers serve on 45 national, European and global society and organisation committees, 8 also serve on the boards of 10 charities, including*:* **The Royal Society** [Morris, Chair, Hooke Committee and URF Biology Panel]; **Royal Society of Edinburgh** [Deary, Chair of Fellowship Committee A1]; **British Neuropsychiatry Association** [Stone, Director 2006–9], **British Neuropsychological Society** [Della Sala, President-elect], **European Association of Neuro-Oncology** [R Grant, President 2004–12], **European Leucodystrophy Association** [ffrench-Constant, Chair], **European Delirium Association** [MacLullich, President], **Federation of European Societies of Neuropsychology** [Della Sala, President 2008–10]. **International Endocrine Foundation** [Leng, President]; **International Union of Basic and Clinical Pharmacology (IUPHAR)** [Harmar, Vice-Chair, Receptor Nomenclature and Drug Classification Database, and Database Chairman]; **Psychonomic Society** [Logie, Chair-elect]; **Scottish Mental Health Research Network** [Lawrie, Director]; **World Stroke Association** [Sandercock, Board of Directors].

Journal Editorships: 23 of our researchers serve on the editorial boards of 51 journals, including **Science** [Morris] and are *Editors-in-Chief* for **Archives of Gerontology & Geriatrics** [Starr], **Cortex** [Della Sala], **Journal of Anatomy** [Gillingwater], **Journal of Memory & Language** [Pickering] and **The Open Critical Care Medicine Journal** [Andrews, 2008].

***Contribution to Scientific and Policy Advisory Boards and Monitoring Committees*:** 24 of our researchers contribute to 57 policy and scientific advisory boards at national and international level, including **UK Biobank** [Sudlow, Chief Scientist; Deary, Neuroscience working group]; **British Paediatric Neurology Surveillance Unit** [Chin]; **British Cohort Studies Scientific Committee**, **MRC Cross-Board Advisory Group** [both Deary]; **National Advisory Committee for Stroke in Scotland** [Dennis, Chair]; **Scottish Government National Dementia Strategies expert panel** [Starr, 2010 & 2013] and **Scottish Dementia Forum** [Starr], **Medical Research Scotland** [Horsburgh, 2006–10]; **NICE Guideline Development Group (Bipolar Disorder)** [Schwannauer]; **Commission on Human Medicine advisory groups** [Owens, Knight]. In the REF period, Sandercock has been the **Chair of the Data Monitoring Committee** (DMC) of 13 International multi-centre randomised controlled trials and a member of an additional 11 DMCs.

Recognition by the Discipline: Deary is a **Fellow of the British Academy** and Morris of the **Royal Society**; seven **Fellows of the Academy of Medical Sciences** [Brophy, Deary, Ironside, Morris, Sandercock, Wardlaw, Will]; ten **Fellows of the Royal Society of Edinburgh**, four elected since 2008 [Brophy, Deary, Della Sala, Grant, Ironside, Leng, Logie, Morris, Pickering, Wardlaw]; Morris is a **Foreign Fellow of the American Academy of Arts and Science; Schilling Research Preis 2013** [Rochefort]; **World Stroke Organisation Presidents Award** [Sandercock, 2012]; **Bhowmick Medal** for contribution to stroke medicine [Dennis and Sandercock, 2012]; **British Society Neuroradiologists President's Medal for Lifetime Contribution to Neuroradiology** [Wardlaw, 2008]; **Jean Hunter Prize for research into nervous disorders from Royal College of Physicians London** [Stone, 2013]; **Worshipful Society of Apothecaries William Farr Medal for Contributions to the Care of the Elderly** [Dennis, 2009]; **Australian CJD Support Group Network 'Champion for CJD Families' Award** [Knight, 2012]; **Biochemical Society Colworth Medal** and the **International Society for Neurochemistry Young Scientist Lectureship Award** [both Hardingham, 2009, 2011]; **Lister Institute Prize** [Lyons, 2012]; **Patrick Wall Medal for Contribution to Pain Research** [Fleetwood-Walker, 2013]; **Mid-Career Prize** from the **Experimental Psychology Society** [Pickering, 2013]; **Distinguished European Personality Psychologist Award** from the **European Association for Personality Psychology** [Deary 2010]; and the **IPSEN Prize for Neuronal Plasticity** [Morris, 2013].